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UNITED STATES DISTRICT COURT

SOUTHERN DISTRICT OF CALIFORNIA

GEN-PROBE INCORPORATED,

Plaintiff,

v.

VYSIS, INC.,

Defendant.

No. 99CV2668H AJB

REPLY SEPARATE STATEMENT OF UNDISPUTED FACTS IN SUPPORT OF PLAINTIFF GEN-PROBE INCORPORATED'S MOTION FOR PARTIAL SUMMARY JUDGMENT OF NON-INFRINGEMENT UNDER THE DOCTRINE OF EQUIVALENTS

DATE: November 19, 2001
TIME: 10:30 a.m.
DEPT.: Court Room 1

HONORABLE MARILYN L. HUFF

Plaintiff Gen-Probe Incorporated ("Gen-Probe") respectfully submits that following Reply Separate Statement of Undisputed Facts in Support of its Motion for Partial Summary Judgment of Non-Infringement Under the Doctrine of Equivalents:

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Undisputed Material Facts And Evidentiary Support Cited In Gen-Probe's Opening Separate Statement	Vysis's Opposition	Gen-Probe's Reply
1. Vysis has previously admitted that TMA is a sequence-specific amplification method and does not use methods of non-specific amplification.	Vysis did not dispute this assertion in its opposition to Gen-Probe's April 30, 2001 Motion for Partial Summary Judgment.	1. Gen-Probe's proffered fact is undisputed.
2. All of the claims of the '338 patent incorporate an "amplification" element. The Court's June 20th Order confirms that each of those claims and incorporated amplification elements literally encompasses only non-specific amplification techniques.	The Court's construction of the claims of the '338 patent is a legal question, not a factual one. Vysis contends that the Court's resolution of that question of law is legally incorrect.	2. Gen-Probe's proffered fact is undisputed.
3. The differences between specific amplification methods and non-specific amplification methods are substantial.	Disputed. See Persing Decl., ¶¶ 5-16.	3. Dr. Persing's declaration does not state that there are only insubstantial differences between methods of specific amplification, such as TMA, and methods of non-specific amplification. Nothing in Dr. Persing's declaration would lead one skilled in the art to

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
		reach such a conclusion. Mullis Reply Decl. at ¶ 5. Rather, Dr. Persing confuses the issue by comparing improperly target capture and non-specific amplification to specific amplification.
4. The methods do not perform the same function in the same way to achieve the same result.	Disputed. See Persing Decl., ¶¶ 5-16.	4. Dr. Persing's declaration does not meaningfully address the "triple identity" test of whether TMA and non-specific amplification "perform substantially the same function in substantially the same way to achieve substantially the same result." Mullis Reply Decl. at ¶ 6. Rather, Dr. Persing confuses the issue by comparing improperly target capture and noon-specific amplification to specific amplification.
5. Gen-Probe's TMA method functions to exponentially	No dispute.	5. Gen-Probe's proffered fact is undisputed.

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
increase both the **absolute** and **relative** amount of a particular nucleic acid sequence of interest in a mixture of nucleic acids.		
6. In direct contrast, non-specific amplification functions only to increase the absolute amount of all nucleic acids present in a sample and does not increase the relative amount of a particular nucleic acid sequence of interest.	In the context of the claims of the '338 patent, the amplification step increases both the absolute and relative amount of the target nucleic acid present in the tested sample. See '338 patent.	6. Vysis does not point to any particular aspect of the '338 patent to support its position and does not dispute the proffered fact. Indeed, it appears that Vysis is confusing the issue by its preface "in the context of the '338 patent." For purposes of the equivalents analysis one must consider the amplification element by itself, not the "invention as a whole" (e.g. other steps that are involved in the claimed invention.) Moreover, there is no evidence that the combination of the target capture step with non-specific amplification methods

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
		can be used to detect small amounts of a target within a clinical sample. Mullis Reply Decl. at ¶10. Moreover, Vysis' expert, Dr. Persing admitted that non-specific amplification does not increase the relative amount of target nucleic acid in a sample. Bowen Decl., Exhibit "1" at 23:3-24:6. Gen-Probe's proffered fact is undisputed.
7. Vysis' own expert has admitted the differences in function between specific amplification and non-specific amplification. [N]on-specific amplification techniques amplify all of the nucleic acid in a sample, both target and non-target nucleic acid. Specific amplification techniques, ***in contrast***, are intended to amplify only the target nucleic acid.	Vysis' expert has not opined that there is no difference between specific and nonspecific amplification techniques, but has the opinion that the differences are insubstantial. See Persing Decl. ¶¶ 5-16.	7. Dr. Persing's declaration does not state that there are only insubstantial differences between methods of specific amplification, such as TMA, and methods of non-specific amplification. Mullis Reply Decl. at ¶ 5. Moreover, Vysis' expert, Dr. Persing, reaffirmed his admission of the differences in his deposition testimony. Bowen Decl.,

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
		Exhibit "1" at 23:3-24:6. Gen-Probe's proffered fact is undisputed.
8. When a particular nucleic acid sequence of interest is contained in a mixture of nucleic acids in a clinical sample, TMA enables a person skilled in the art to exponentially copy the sequence of interest.	No dispute.	8. Gen-Probe's proffered fact is undisputed.
9. This makes it easy to determine whether or not a pathogenic microorganism is hiding among millions of other organisms in a patient sample.	No dispute.	9. Gen-Probe's proffered fact is undisputed
10. Specific amplification is useful for diagnostic purposes even without a target capture step. In contrast, non-specific amplification is *not* a viable diagnostic method because it does not increase the amount of a target nucleic acid relative	Vysis disputes that non-specific amplification is "not a viable diagnostic method." Non-specific amplification is a viable diagnostic method when used in the context of claims of the '338 patent. May 25, 2001 Persing Decl., ¶ 11.	10. Vysis' use of the phrase "in the context of the claims of the '338 patent" is erroneous under the so-called "all elements" rule. In any event, specific amplification methods, such as TMA and PCR, are useful for diagnostic

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
to everything else. Vysis' own expert witness has admitted this important distinction: Without the use of target capture prior to amplification, ***non-specific amplification would not be a viable technique for detecting target nucleic acids in a sample*** because, as pointed out in the quoted paragraph, non-specific amplification causes the replication of virtually any nucleic acid sequence, including other irrelevant nucleic acids in the sample.		purposes even without a target capture step. Mullis Reply Decl. at ¶ 10-12. Non-specific amplification methods, such as those suggested in the '338 patent, are not useful diagnostic methods, with or without a target capture step. Mullis Reply Decl. at ¶ 10-12. Vysis' expert, Dr. Persing, admitted that he is not aware of any commercially approved non-specific method of amplification. Bowen Decl., Exhibit "1" at 30:8-18. Gen-Probe's proffered fact is undisputed.
11. Therefore, Dr. Persing has admitted that "without the invention [i.e., the combination of a preliminary "target capture" step with amplification], ***only specific amplification could be used."***	Vysis disputes that the quoted section of Dr. Persing's May 25, 2001 Declaration was based on the assertions in Gen-Probe's Undisputed Fact No. 10.	11. Vysis does not present any evidence to dispute the admission of Dr. Persing on this point. Hence, Gen-Probe's proffered fact is undisputed. *See also* Reply Fact No. 10.

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
12. The enzymes and primers used in any amplification process can be specific or non-specific.	No dispute.	12. Gen-Probe's proffered fact is undisputed
13. The primers used in Gen-Probe's specific TMA amplification method have been carefully selected by Gen-Probe's scientists and are generally designed to bind to specific, unique sequences in a DNA or RNA molecule.	No dispute.	13. Gen-Probe's proffered fact is undisputed
14. In amplification processes, sequence-specific primers and enzymes such as those used in TMA play a role substantially different from non-specific primers and enzymes.	Disputed. See Persing Decl., ¶¶ 10-16.	14. Dr. Persing's declaration does not address this fact. Rather, Dr. Persing improperly confuses the issue by speaking in terms of the "context" of the '338 patent. The role of sequence-specific primers and enzymes, such as those used in MA, play a substantially different role and achieve substantially different results from non-specific primers and

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
		enzymes. Mullis Reply Decl. at ¶¶3, 12-14.
15. This fact is well known to those of ordinary skill in the art.	Disputed. See Persing Decl., ¶¶ 10-16.	15. Dr. Persing's declaration does not address this fact. *See* Mullis Reply Decl. at ¶3-7. Gen-Probe's proffered fact is undisputed.
16. For example, specific primers and enzymes can function together to amplify a target nucleic acid only if the specific sequence of interest bound by the primer and/or recognized by the enzymes is present in the sample.	Disputed. All nucleic acid amplification techniques have some degree of nonspecificity. See Persing Decl., ¶ 6.	16. Persons of ordinary skill in the art know and understand that all nucleic acid amplification techniques have some degree of non-specificity. They also know that this ancillary and limited degree of non-specificity is immaterial to determining whether specific amplification techniques are equivalent to non-specific amplification. When persons of ordinary skill in the art employ methods of sequence-specific amplification, such as TMA and PCR, those methods are

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
		extremely specific as compared with amplification using random hexamer primers and non-specific enzymes. The difference in specificity is like the difference between night and day. PCR and TMA are both 1 million times more specific than any non-specific amplification system, and the consequences of this difference are both substantial and absolute. The fact that TMA and PCR may result in some very limited amount of amplification of non-target sequences does not render those sequence-specific methods the equivalent of non-specific amplification methods with random hexamer primers and non-specific enzymes, which are deliberately designed to be totally non-

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
		specific. Mullis Reply Decl. at ¶¶ 7-8.
17. By contrast, non-specific primers and enzymes will amplify *any* and *all* sequences present in the sample.	No dispute.	17. Gen-Probe's proffered fact is undisputed
18. The random primers will bind to all of the sequences in the sample and non-specific replication enzymes will catalyze DNA synthesis at points throughout the entire lengths of the nucleic acid molecules present without regard to sequence.	No dispute.	18. Gen-Probe's proffered fact is undisputed
19. In its TMA method, Gen-Probe uses two amplification enzymes that depend upon the presence of specific primers.	No dispute.	19. Gen-Probe's proffered fact is undisputed
20. One of these enzymes is reverse transcriptase ("RT").	No dispute.	20. Gen-Probe's proffered fact is undisputed
21. RT is a DNA polymerase that produces a complementary DNA strand	No dispute.	21. Gen-Probe's proffered fact is undisputed

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
copy of a single-stranded RNA or DNA that has a bound primer.		
22. In TMA, RT produces complementary DNA from the target nucleic acids (or their complementary strands) only if the sequence-specific primers first bind to a single strand of RNA or DNA.	No dispute.	22. Gen-Probe's proffered fact is undisputed
23. If the target organism is not present in the sample, the primers will be unable to bind to the captured sequence and the RT will not initiate synthesis.	Disputed. All nucleic acid amplification techniques have some degree of nonspecificity. See Persing Decl., ¶ 6.	23. Persons of ordinary skill in the art know and understand that all nucleic acid amplification techniques have some degree of non-specificity. Mullis Reply Decl. at ¶¶ 7-8. The non-specific products of PCR and TMA do not affect the overall specificity of the processes. The primary product of specific amplification is identified by its precisely defined length and the

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		presence of amplified internal target sequences. Spuriously amplified sequences, when they occur, are only rarely the same size as the target-specific product. Furthermore, spuriously amplified sequences, when they occur, do not contain internal sequences that are homologous to target-specific hybridization probes. Therefore, it is easy to distinguish the spuriously-amplified products. Mullis Reply Decl. at ¶ 9.
24. Another specific primer used in Gen-Probe's method also includes a specific "promoter" sequence that is recognized by another enzyme ("T7 RNA polymerase") that binds specifically to that promoter sequence to produce	No dispute.	24. Gen-Probe's proffered fact is undisputed

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
many RNA copies by transcription.		
25. A function "T7 promoter" is formed in the course of the TMA process if, and only if, (1) the primer finds and binds to its complementary target sequence in the captured target molecule so that the target sequence is copied by reverse transcriptase and (2) the second primer binds to the newly synthesized DNA and DNA polymerase makes the complementary DNA strand.	Disputed. All nucleic acid amplification techniques have some degree of nonspecificity. See Persing Decl., ¶ 6.	25. Vysis' Opposition does not address this fact. *See* Gen-Probe's Reply Undisputed Facts Nos. 16 and 23.
26. If this double-stranded, and hence functional, T7 promoter *is* formed as a result of these *two* primer binding and extension processes, then the T7 RNA polymerase used in Gen-Probe's HIV/HCV test will amplify the sequence attached to the T7 promoter	No dispute.	26. Gen-Probe's proffered fact is undisputed

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
sequence.		
27 The T7 RNA polymerase does not amplify other sequences present in the sample because they are not attached to a T7 promoter sequence.	Disputed. All nucleic acid amplification techniques have some degree of nonspecificity. See Persing Decl., ¶ 6.	27. *See* Gen-Probe's Reply Undisputed Facts Nos. 16 and 23.
28. Thus, in Gen-Probe's HIV/HCV test, the T7 polymerase enzyme *specifically* recognizes the T7 promoter sequence, which has been *specifically* attached to the target sequence by the binding of *specific* primers, and the T7 polymerase *specifically* amplifies only that sequence.	Disputed. All nucleic acid amplification techniques have some degree of nonspecificity. See Persing Decl., ¶ 6.	28. *See* Gen-Probe's Reply Undisputed Facts Nos. 16 and 23.
29. The process repeats in a cyclic fashion, only amplifying the particular target sequence of interest.	Disputed. All nucleic acid amplification techniques have some degree of nonspecificity. See Persing Decl., ¶ 6.	29. *See* Gen-Probe's Reply Undisputed Facts Nos. 16 and 23.
30. Gen-Probe's amplification method therefore safeguards	Disputed. All nucleic acid amplification techniques have	30. *See* Gen-Probe's Reply Undisputed Facts Nos. 16 and

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
against amplification of non-target sequences and thus protects against false positive results.	some degree of nonspecificity. See Persing Decl., ¶ 6.	23.
31. TMA functions in way that is substantially different than the way in which non-specific amplification functions.	Disputed. See Persing Decl., ¶¶ 9-16.	31. None of the statements in Dr. Persing's declaration is material to considering whether there are substantial differences between TMA and non-specific amplification. One of ordinary skill in the art would conclude that there are substantial differences between Gen-Probe's TMA method and the non-specific amplification methods described and claimed in the '338 patent. Sequence-specific amplification methods such as TMA do not perform substantially the same function in substantially the same way to achieve substantially the same result as non-specific

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
		methods of amplification. Mullis Reply Decl. at ¶ 16.
32. Specific amplification methods commonly achieve ***exponential*** amplification of the target sequence, as compared with linear amplification.	Disputed. Specific amplification methods can achieve either linear or exponential amplification, depending on the reaction conditions and the techniques employed. Vysis requires discovery from Gen-Probe's expert to provide further support for its dispute of this fact.	32. Gen-Probe's proffered fact remains undisputed. Vysis has conducted its discovery and cites to no evidence to refute the proffered fact.
33. Sustained, significant, exponential amplification is a hallmark of specific amplification methods.	Disputed. Specific amplification methods can achieve either linear or exponential amplification, depending on the reaction conditions and the techniques employed. Vysis requires discovery from Gen-Probe's expert to provide further support for its dispute of this fact.	33. Gen-Probe's proffered fact remains undisputed. Vysis has conducted its discovery and cites to no evidence to refute the proffered fact.

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
34. In contrast, the non-specific amplification methods of Examples 4 and 5 of the '338 patent admittedly achieve only linear amplification, not exponential amplification.	No dispute.	34. Gen-Probe's proffered fact is undisputed.
35. The non-specific amplification methods of Examples 5 and 6 also cannot achieve exponential amplification. Because random primers bind at various places along the nucleic acids present in the sample, the products of amplification are fragmented.	Disputed. Example 6 of the '338 patent discloses a technique for achieving exponential amplification of a target nucleic acid. ('338 patent, col. 31, line 55 to col. 32, line 7.)	35. Gen-Probe's proffered fact remains undisputed. Vysis submits no evidence to refute that of Dr. Mullis in his September 26, 2001 Declaration at ¶41.
36. If these products were then subjected to another round of non-specific amplification, the resulting products would be smaller still.	Disputed.	36. Vysis submits no evidentiary support for its claimed "dispute". Hence, Gen-Probe's proffered fact remains undisputed.
37. Multiple rounds of non-specific amplification thus	Disputed. Vysis requires discovery from Gen-Probe's	37. Vysis submits no evidentiary support for its

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diminish rapidly in efficiency, whereas multiple rounds of specific amplification produce extraordinarily large amounts of full size product nucleic acids in very short periods of time.	expert to provide further support for its dispute of this fact.	claimed "dispute". Hence, Gen-Probe's proffered fact remains undisputed.
38. Non-specific amplification using random hexamer primers results in fragmented nucleic acids, each of which contains the random sequences present in the primers.	No dispute.	38. Gen-Probe's proffered fact is undisputed.
39. The resulting products are thus heterogeneous and have undefined composition.	Disputed.	39. Vysis submits no evidentiary support for its claimed "dispute". Hence, Gen-Probe's proffered fact remains undisputed.
40. Such nucleic acids are unsuitable for most of the purposes for which homogeneous, specifically amplified nucleic acids of known composition are	Disputed. In the context of the claimed invention, non-specific amplification techniques can amplify target nucleic acids in a manner sufficient to permit their	40. Vysis attempt to preface its position with the phrase "in the context of the claimed invention" is improper and in violation of the "all elements" rule. In any event, non-

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
employed.	detection as part of a diagnostic assay.	specific amplification methods, such as those suggested in the '338 patent, are not useful diagnostic methods, with or without a target capture step. Mullis Reply Decl. at ¶ 10.
41. As a result, Gen-Probe's TMA method also does not yield the same result as that obtained with non-specific amplification.	Disputed. See Persing Decl., ¶¶ 9-16.	41. Dr. Persing's declaration suggests that TMA and the non-specific amplification method of Example 5 of the '338 patent both result in the creation of a double-stranded DNA, and this double-stranded DNA constitutes the "same result" from each process. This statement is not true. The mere fact that both products are double-stranded DNA is immaterial to one skilled in the art. What is important is the content of the double-stranded DNA. The double-stranded product of the amplification

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
		method of Example 5 would be a heterogeneous collection of fragments containing a mixture of sequences present in the original sample. Whether or not the collection of fragments contains any sequences of a specific target is unknown. In contrast, PCR and TMA produce discrete products of known size and composition. Both the absolute and relative amounts of the specific target sequence are increased millions-fold, allowing the detection of even a single molecule of target within millions of molecules of non-target sequence. Mullis Reply Decl. at ¶ 11. Vysis' expert, Dr. Persing, admitted that even employing the method of Example 5's "alternative" capture probe

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
		method could result in non-specific replication of DNA. Bowen Decl., Exhibit "1" at ¶114:20-24.
42. The Court has previously noted that the specification of the '338 patent contains no reference to any specific amplification techniques. To the contrary, the specification clearly suggests that the claimed amplification techniques of the invention don't require the use of specific primers necessary for specific amplification.	Vysis disputes the implication that specific amplification techniques are excluded from the claims of the '338 patent.	42. Vysis submits no evidentiary support for its claimed "dispute". Hence, Gen-Probe's proffered fact remains undisputed.
43. This absence in the '338 patent of any disclosure of specific amplification techniques was not accidental or unintended. To the contrary, Gene-Trak Systems, Vysis' predecessor-in-interest, and its employed inventors	Vysis disputes there is an absence of any disclosure of specific amplification in the '338 patent. Vysis does not dispute that Dr. Lawrie made the quoted statements in his deposition, but disputes the relevance of those statements	43. Vysis submits no evidentiary support for its claimed "dispute". Hence, Gen-Probe's proffered fact remains undisputed.

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
were well aware of the specific amplification techniques such as PCR. In fact, the admitted focus of the inventors' effort leading to the disclosure in the '338 patent was to find something "different" from specific amplification. For example, inventor Jon Lawrie testified that the patent was meant to cover new amplification methods using non-specific primers, not already-known methods such as PCR: Q. Can you recall any reason that a reference to PCR might have been intentionally omitted from the patent application? A. Yes.... Q. If there's no reference in the ['338] patent to combining target capture with PCR, do you have any explanation as to why it is not there? A. I believe that it was a separate, the thought behind this [referring to the	to the determination of infringement under the doctrine of equivalents.	

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
'338 patent] was coming up with new methods of amplification, not old ones. Q. For the purposes of what you just said you classify PCR as an old method of amplification? A. PCR itself was described in the patent, issued patent [e.g., it was an "old" method]. Q. And your understanding of the 338 patent was that it was directed to other methods of amplification? A. The, it was, it was directed to the methods disclosed by, you know, the *methods separate from PCR.*		
44. Inventor King also stated the inventors' purpose and also distinguished non-specific amplification from PCR: Q. From a high level perspective, what were the discussion topics addressed during this meeting? A. I think that at the highest level we were looking for amplification methods ***that did not involve PCR amplification***. (King Depo. At 45: 10-15 (emphasis added).) Q. Okay. So the purpose -- the general purpose of	Vysis does not dispute that Dr. King made the quoted statements in his deposition, but disputes the relevance of those statements to the determination of infringement under the doctrine of equivalents.	44. Gen-Probe's proffered fact is undisputed.

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
the discussion as I understand it that took place at Gene-Trak among the four doctors was to identify -- in general identify an amplification technique that would amplify low concentrations of target nucleic acids in a sample, correct? A. Yes. Q. And as I understand your testimony, you wanted to find a technique ***that was different from PCR***, correct? A. Yes.		
45. As this testimony suggests, PCR was well known to the inventors and the scientific community at large. Dr. Kary Mullis invented PCR in 1983, for which he received the Nobel Prize in Chemistry. Dr. Mullis and his colleagues publicly described PCR at a scientific meeting in the summer of 1985 and published their discovery in December 20, 1985.	No dispute.	45. Gen-Probe's proffered fact is undisputed.
46. James Richards, Gene	No dispute.	46. Gen-Probe's proffered

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
Trak's Director of Business Development and Licensing, admits that, within the scientific community, PCR was immediately "big news."		fact is undisputed.
47. One of the reasons that the '338 inventors sought to find something "different" from specific amplification techniques such as PCR was due to Gene Trak's concern that it could not obtain a license from Cetus Corp. to use PCR. Cetus Corporation, which employed Dr. Mullis, originally owned the rights to PCR. Gene-Trak sought a license from Cetus, but its requests were rejected.	No dispute.	47. Gen-Probe's proffered fact is undisputed.
48. The view of the fundamental difference between non-specific and specific amplification techniques was shared not only	Vysis disputes the statement that there is a "fundamental difference between non-specific and specific amplification techniques." See	48. Vysis' expert, Dr. Persing's declaration does not address this fact. Rather, Dr. Persing improperly confuses the issue by referring to the

UNDISPUTED MATERIAL FACTS AND EVIDENTIARY SUPPORT CITED IN GEN-PROBE'S OPENING SEPARATE STATEMENT	VYSIS'S OPPOSITION	GEN-PROBE'S REPLY
between the inventors but with Gene-Trak scientific management as well. In particular, in a letter he wrote in 1989, Dr. Richards, pointedly contrasted the '338 patent's method of non-specific amplification with other known specific methods that used specific primers or promoters: Cetus, Sibia/Salk, Biotechnica, etc. all claim specific primers for amplification *whereas the present invention claims uses of the* opposite, namely, non-specific primer or promoters....	Persing Decl., ¶¶ 5 -16. Vysis also disputes that the independent claims of the '338 patent ever recited non-specific primers or promoters.	"context" of the '338 patent rather than the element of amplifying. Nothing in Dr. Persing's declaration refutes the testimony cited by Gen-Probe in support of this fact and it remains undisputed. Moreover, Dr. Persing admitted in his deposition testimony that substantial and fundamental differences exist between specific and non-specific methods of amplification. Bowen Decl., Exhibit "1" at 23:3-24:6; 25:19-26:21; 30:8-18; 57:8-58:18; 61:20-62:13.

Dated: November 13, 2001

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